

AMENDMENT: IN THE CLAIMS

Please amend the claims as noted below, without prejudice to subsequent renewal. The listing of claims below replaces all prior versions, and listings, of claims in the application.

These amendments introduce no new matter and support for the amendment is replete throughout the specification and claims as originally filed. These amendments are made without prejudice and are not to be construed as abandonment or dedication of the previously claimed subject matter, or agreement with any objection or rejection of record.

Listing of Claims:

1-105. (Cancelled)

106. (Original) A method of determining a compound that is a modulator of Y receptor associated differentiation of a mesenchymal stem cell (MSC) or bone marrow stromal cell (BMSC) into an osteoblast-type cell comprising:

- (i) culturing a MSC or BMSC in the presence of a candidate compound;
- (ii) culturing a MSC or BMSC in the absence of the candidate compound; and
- (iii) determining Y receptor activity and/or expression and the number of differentiated osteoblast-type cells at (i) and (ii), wherein a modified number of osteoblast-type cells and a modified Y receptor activity and/or expression at (i) and (ii) indicates that the compound is a modulator of Y receptor associated differentiation of an osteoblast-type cell.

107. (Original) A method of determining a compound that is a modulator of Y receptor associated differentiation of a mesenchymal stem cell (MSC) or bone marrow stromal cell (BMSC) into an adipocyte-type cell comprising:

- (i) culturing a MSC or BMSC in the presence of a candidate compound;
- (ii) culturing a MSC or BMSC in the absence of the candidate compound; and
- (iii) determining Y receptor activity and/or expression and the number of differentiated adipocyte-type cells at (i) and (ii), wherein a modified number of adipocyte-type cells and a modified Y receptor activity and/or expression at (i) and (ii) indicates that the

compound is a modulator of Y receptor associated differentiation of an adipocyte-type cell.

108-121. (Cancelled)

122. (Currently amended) A non-naturally occurring transformed animal having reduced expression of multiple Y receptors in a cell or tissue by virtue of carrying insertions in multiple Y receptor-encoding genes wherein said animal has modulated bone remodeling activity, modulated bone growth activity or modulated adiposity compared to an otherwise isogenic animal that does not carry the insertions.

123-124. (Cancelled)

125. (Currently amended) The non-naturally occurring transformed animal according to claim 122~~any one of claims 122 to 124~~ wherein the multiple Y receptor encoding genes carrying the insertions are selected from the group consisting of:

- (i) a Y1 receptor and a Y2 receptor;
- (ii) a Y1 receptor and a Y5 receptor;
- (iii) a Y1 receptor and a Y7 receptor;
- (iv) a Y2 receptor and a Y5 receptor;
- (v) a Y2 receptor and a Y7 receptor;
- (vi) a Y5 receptor and a Y7 receptor;
- (vii) a Y1 receptor and a Y2 receptor and a Y5 receptor;
- (viii) a Y1 receptor and a Y2 receptor and a Y7 receptor;
- (ix) a Y1 receptor and a Y5 receptor and a Y7 receptor; and
- (x) a Y1 receptor and a Y2 receptor and a Y5 receptor and a Y7 receptor.

126. (Currently amended) The non-naturally occurring transformed animal according to claim 122~~any one of claims 122 to 124~~ wherein the multiple Y receptor encoding genes carrying the insertions are selected from the group consisting of:

- (i) a Y1 receptor and a Y2 receptor;
- (ii) a Y2 receptor and a Y4 receptor; and
- (iii) a Y1 receptor and a Y2 receptor and a Y4 receptor.

127. (Currently amended) The non-naturally occurring transformed animal according to claim 122~~any one of claims 122 to 126~~ wherein the animal is a mouse.

128. (Currently amended) A progeny animal of the non-naturally occurring transformed animal according to claim 122~~any one of claims 122 to 127~~ wherein said progeny animal has reduced expression of multiple Y receptors in a cell or tissue by virtue of carrying insertions in multiple Y receptor-encoding genes.

129-138. (Cancelled)

139. (Original) A method of treatment of aberrant bone remodeling in a subject in need thereof comprising isolating a mesenchymal stem cell (MSC) or bone marrow stromal cell (BMSC) from a human or animal subject, treating the MSC or BMSC with a compound that modulates Y receptor associated differentiation under conditions sufficient to induce differentiation of the MSC or BMSC into an osteoblast type cell and introducing the osteoblast type cell into the subject in need of treatment.

140-150. (Cancelled)

151. (New) A method comprising administering a compound to the non-naturally occurring transformed animal of claim 122 and determining bone remodeling activity, bone growth or adiposity of the animal to thereby determine an effect of the compound on bone remodeling activity, bone growth or adiposity.

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152. (New) The method of claim 151 wherein the non-naturally occurring transformed animal has reduced expression of a Y4 receptor in a cell or tissue by virtue of carrying an insertion in the Y4 receptor-encoding gene.